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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,860	10/19/2005	Marc K. Hellerstein	416272003600	5469

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
10/08/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,860	HELLERSTEIN, MARC K.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20,23,24,26,27 and 29* is/are pending in the application.

4a) Of the above claim(s) *14-20,23,24,26 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/28/08 has been entered. Claims 1-20, 23, 24, 26, 27 and 29 and pending. Claims 14-20, 23, 24, 26 and 27 are withdrawn from consideration being drawn to non-elected subject matter. Claims 1-13 and new claim 29 are under examination.

Claims Summary

2. The claims as amended are drawn to a method of determining the rate of replication (growth) or destruction (death) of an infectious agent while they are in a host organism. The method allows the *in vivo* assessment of microbial growth (see specification page 6, first full paragraph, last sentence). The method steps include, but are not limited to the following:

a. Administering an isotope-labeled precursor molecule to the host to allow the molecule to become incorporated into a biochemical component of the infectious agent in the host;

b. Obtaining a sample(s) from the host that comprises the biochemical component of the infectious agent;

c. Isolating the biochemical component of the infectious agent from the sample(s); in one embodiment (claim 29) the separation is performed by ultracentrifugation;

d. Measuring isotopic content, rate of change of isotopic content, and/or pattern or rate of change of pattern of said isotopic content in the biochemical component; and

e. Calculating rate of synthesis or breakdown of the biochemical component to determine the rate of replication or destruction of the infectious agent in the host.

Paragraph [0066] of the published application, USPGPUB 20060105339 A1, discloses that the term " 'isolating' refers to separating one component from one or more additional components in a mixture of components. For example, isolating a biochemical component refers to separating one biochemical components from a mixture of biochemical components. Small quantities of additional biochemical components may be present in the isolated biochemical component."

Specifically, the sample is a tissue or bodily fluid, such as urine, blood, saliva, etc., see the list in claim 13. The host organism is a mammal, including humans. The infectious agent is any of bacteria, viruses (HIV, HBV, HCV, or other clinically important virus), protozoa, yeast and parasites. The precursor molecule is any molecule utilized in one or more specific biochemical pathways to produce a biochemical component of an infectious agent (page 10, first full paragraph). Examples of isotope-labeled precursor molecules are $^{2}H_{2}0$, ^{2}H-glucose, ^{2}H-labeled amino acids, etc. The biochemical component is a constituent part of an infectious agent that is synthesized from precursor molecules, such as DNA, RNA, proteins, lipids, carbohydrates or porphyrins (page 10, second full paragraph). The isotopic label is selected from the group consisting of ^{13}C, ^{14}C, ^{2}H, ^{3}H, ^{15}N, ^{35}S, ^{11}C and ^{35}P. Measurement of isotopic content is performed via mass spectrometry.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-13 remain rejected under 35 U.S.C. 102(b) as being anticipated by Hellerstein (US Patent 6,010,846, "Hellerstein"). The claims are summarized above. Hellerstein discloses a method for measuring cellular proliferation and destruction rates using isotope labels (abstract). The isotope-labeled precursor molecules are administered to human subjects (col. 13, section 5.3.2). For example, ^{2}H-glucose (precursor of deoxyribose) is administered to an HIV-infected subject and the label is incorporated into the subject's DNA to measure cellular proliferation and/or destruction. Although Hellerstein's disclosure does not teach that the ^{2}H-glucose is a precursor of the deoxyribose that is incorporated into the proviral DNA of HIV, this is expected. Since Hellerstein suggests the administration of ^{2}H-glucose to HIV-infected patients, Hellerstein's patient population and the patient population on the instantly claimed methods are the same. By performing Hellerstein's method for the *in vivo* assessment of T cell proliferation/destruction, one would also inherently be performing the instantly claimed method because the extraction of DNA from T cells is expected to also extract DNA from HIV proviral DNA in infected T cells. Hellerstein's separation of T cells (containing HIV DNA) from blood (biological sample) meets the claim limitation represented in step c) of the claims. Hellerstein discloses that cells can be optionally further purified prior to extracting the DNA using a variety of techniques, including density gradient centrifugation (col. 12, first full paragraph). The mass

spectrometry step disclosed in Hellerstein (see claims) for the purpose of tracking rates of T cell proliferation/destruction is expected to also track the rate of HIV proliferation/destruction. Therefore, the method as claimed is anticipated by Hellerstein.

Applicant's arguments have been carefully considered but fail to persuade. Applicant argues that the isolation step c) in the claims is not taught by Hellerstein.

In response to Applicant's arguments, the Office has considered the scope of the claims and in particular, the meaning of "isolating" as defined by the specification. Step c) of the claims requires that the biochemical component of the infectious agent be separated from the biological sample. The biological sample is not limited to any particular component. For example, in claim 2, the sample is tissue; in claim 3, the sample is bodily fluid. These limitations do not require separation of viral DNA (or any other pathogen's DNA) from cellular DNA, which is why Hellerstein's separation of T cells (containing both viral and host DNA) from blood (bodily fluid) meets the limitation of step c) in the instant claims. The Office cannot read any meaning into the term "isolating" without further clarification as to what the component is isolated away from.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hellerstein (US Patent 6,010,846, "Hellerstein"). The claim is directed to an embodiment wherein the isolating

step c) is accomplished by ultracentrifugation. Hellerstein discloses that cells can be optionally further purified prior to extracting the DNA using a variety of techniques, including density gradient centrifugation (col. 12, first full paragraph). It may well be that the density gradient centrifugation that is taught in Hellerstein is actually density gradient ultracentrifugation, however, the term "ultracentrifugation" is not specifically mentioned.

It would have been obvious to one of ordinary skill in the art to use any technique known in the art to isolate DNA, including ultracentrifugation (centrifugation in a vacuum-type centrifuge). Given that the ultracentrifuge was well known to the ordinary artisan at the time of the invention, it would have been obvious to select an ultracentrifuge as opposed to a non-vacuum centrifuge (if that is even what was meant in the Hellerstein patent). One would have been motivated to use the vacuum-type centrifuge in order to improve separation of components. Therefore, the embodiment of claim 29 would have been obvious in light of Hellerstein's teachings and the knowledge of the ordinary artisan regarding the art of ultracentrifugation.

Conclusion

5. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30), alternate Fridays off,. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Stacy B. Chen/
Primary Examiner, TC1600